EXHIBIT B

American National Standard

ANSI/AAMI/ISO 5840:2005

Cardiovascular implants—Cardiac valve prostheses

AAMI
ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION

ISO 14937:2000, *Sterilization of health care products—General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices*

ISO 14971:2000, *Medical devices—Application of risk management to medical devices*

EN 12442-1, *Animal tissues and their derivatives utilized in the manufacture of medical devices—Part 1: Analysis and management of risk*

EN 12442-2, *Animal tissues and their derivatives utilized in the manufacture of medical devices—Part 2: Controls on sourcing, collection and handling*

EN 12442-3, *Animal tissues and their derivatives utilized in the manufacture of medical devices—Part 3: Validation of the elimination and/or inactivation of viruses and transmissible agents*

Guidelines for reporting morbidity and mortality after cardiac valvular operations, American Association for Thoracic Surgery, European Association for Cardiothoracic Surgery, Society of Thoracic Surgeons, *Annals of Thoracic Surgery*, 62, pp. 932–935, 1996

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1 accessories: Device-specific tools that are required to assist in the implantation of the heart valve substitute.

3.2 actuarial: Statistical technique for estimating survival curves prior to the death of the last member of a cohort.

NOTE—Some examples are the "Kaplan-Meier" technique and the "life-table" technique.

3.3 anticoagulant-related hemorrhage: Internal or external bleeding that causes death or stroke, or that requires transfusion, operation, or hospitalization.

NOTE—This definition is restricted to patients who are receiving anticoagulants and/or antiplatelet drugs, and excludes minor bleeding events.

3.4 arterial diastolic pressure: Minimum value of the arterial pressure during diastole.

3.5 arterial peak systolic pressure: Maximum value of the arterial pressure during systole.

3.6 back pressure: Differential pressure applied across the closed valve.

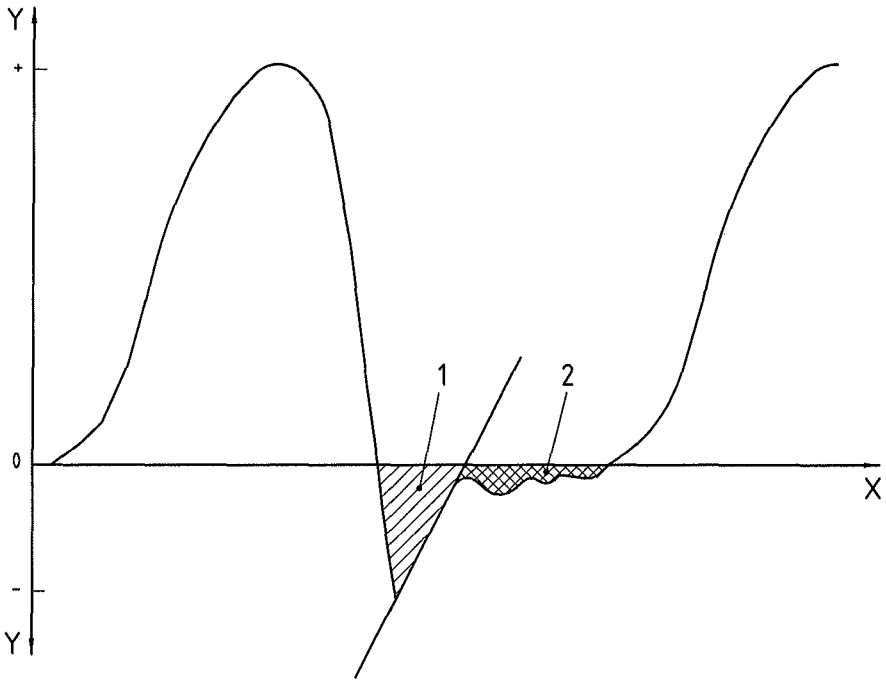
3.7 blood-equivalent fluid: Fluid whose physical properties, e.g., specific gravity, viscosity, approximate those of blood.

3.8 closing volume: Component of the regurgitant volume that is associated with the dynamics of valve closure during a single cycle.

See Figure 1.

3.9 control valve: Heart valve substitute for preclinical and clinical evaluations of similar design and constructed of similar material as the investigational device.

NOTE—The control valve should have a known clinical history.



Key
X time
Y flowrate
1 closing volume
2 leakage volume

Figure 1—Example of flow waveform and regurgitant volumes for one cycle

3.10 cumulative incidence: Statistical technique where events other than death can be described by the occurrence of the event over time without including death of the subjects.

NOTE—Cumulative incidence is also known as "actual" analysis.

3.11 cycle: One complete sequence in the action of a heart valve substitute under pulsatile-flow conditions.

3.12 cycle rate: Number of complete cycles per unit of time, usually expressed as cycles per minute (cycles/min).

3.13 design verification: Establishment by objective evidence that the design output meets the design input requirements.

3.14 design validation: Establishment by objective evidence that device specifications conform with user needs and intended use(s).

3.15 effective orifice area: A_{EO}, orifice area that has been derived from flow and pressure or velocity data.

3.16 failure: Inability of a device to perform its intended function at any point during its intended lifetime.

NOTE—The inability to perform the intended function may manifest itself as a reduced operating effectiveness and/or as hazards.

3.17 failure mode: Mechanism of failure which can result in a hazard.

NOTE—Stent fracture, calcification, and prolapse are examples of failure modes.

3.18 flexible heart valve substitute: Heart valve substitute wherein the occluder is flexible under physiological conditions.

NOTE—The orifice ring may or may not be flexible. This category was previously known as biological heart valve substitute because of the biological source of the flexible occluder(s) but, at a minimum, should also include flexible polymer occluder(s).

3.19 forward-flow phase: Portion of the cycle time during which forward flow occurs through a heart valve substitute.

3.20 hazard: Known or potential source of harm which results from a given failure mode.

3.21 harm: Physical injury or damage to the health of the patient or end-user of the device.

NOTE—Adapted from ISO/IEC Guide 51:1999[14], definition 3.3.

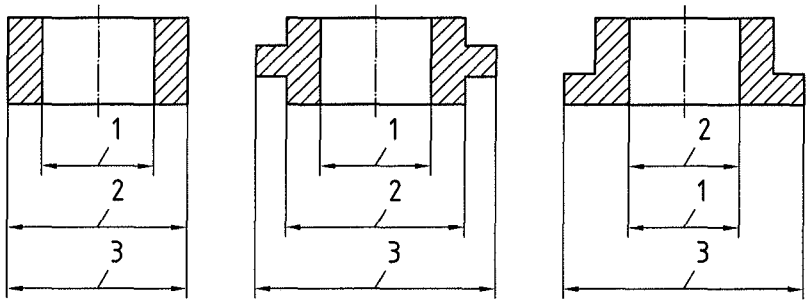
3.22 heart valve substitute: Device used to replace or supplement a natural valve of the heart. See also 3.18 and 3.48, and examples in Figures J.1, J.2, J.3, J.4, and J.5.

3.23 intended use: Use of a product, process, or service in accordance with the specifications, instructions, and information provided by the manufacturer.

3.24 internal orifice area: Numerical indication of the area within a prosthetic heart valve through which blood flows. See Figure 2.

3.25 intra-annular sewing ring: Sewing ring designed to secure the heart valve wholly or mostly within the patient's tissue annulus. See Figure 2. See also 3.24, 3.66, and 3.70.

3.26 intrasupra-annular sewing ring: Sewing ring designed to secure a portion of the valve or sewing ring above the patient's tissue annulus and also some portion of the valve within the patient's tissue annulus. See Figure 2. See also 3.24, 3.66, and 3.70.



intra-annular **intrasupra-annular** **supra-annular**

Key
1 IOA
2 TAD
3 ESRD

Figure 2—Designation of dimensions of heart valve substitute sewing ring configurations

3.27 isolated (aortic or mitral) heart valve substitute: Implantation of single heart valve substitute excluding patients who have a second heart valve substitute in a different anatomical position.

NOTE—Concomitant procedures, including valve repair, coronary artery bypass, and ascending aortic aneurysm repair, are not relevant to this definition. See 7.4.4.

3.28 leakage volume: Component of the regurgitant volume which is associated with leakage through the closed valve during a single cycle.

NOTE—The point of separation between the closing and leakage volumes is obtained according to a defined and stated criterion (the linear extrapolation shown in Figure 1 is just an example).

3.29 linearized rate: Linearized rate for a complication is the total number of events divided by the total time under evaluation.

NOTE—Generally, the rate is expressed in terms of percent per patient year.

3.30 long-term follow-up: Continued (after regulatory approval) periodic assessment of patients who have received the heart valve substitute during the clinical evaluation.

3.31 manufacturer: Organization with responsibility for the design, manufacture, packaging, or labeling of a medical device, assembling a system, or adapting a medical device before it is placed on the market, regardless of whether these operations are carried out by the organization or on their behalf by a third party.

3.32 mean arterial pressure: Time-averaged arithmetic mean value of the arterial pressure during one cycle.

3.33 mean pressure difference: Time-averaged arithmetic mean value of the pressure difference across a heart valve substitute during the forward-flow phase of the cycle.

NOTE—The use of "mean pressure gradient" for this term is deprecated.

3.34 nonstructural dysfunction: Abnormality resulting in stenosis or regurgitation of the heart valve substitute that is not intrinsic to the valve itself.

NOTE—This dysfunction is exclusive of valve thrombosis, systemic embolus, or infection diagnosed at re-operation, autopsy, or *in vivo* investigation. Examples include entrapment by pannus or suture, paravalvular leak, inappropriate sizing, and significant hemolytic anemia.

3.35 occluder: Component(s) of a heart valve substitute, such as rigid or flexible leaflets, discs, and balls, that move(s) to inhibit backflow.

NOTE—The occluders of flexible heart valve substitutes are typically called "leaflets" or "cusps".

3.36 operative mortality: Death from any cause during operation or within 30 d of the operation.

3.37 outflow tract profile height: Maximum distance that the valve extends axially into the outflow tract in the open or closed position, whichever is greater, measured from the valve structure intended to mate with the top (atrial or aortic side) of the patient's annulus.

3.38 pannus: Ingrowth of tissue into the heart valve substitute which may interfere with normal functioning.

3.39 paravalvular leak: Clinically or hemodynamically detectable defect between the heart valve substitute and the patient's annulus.

NOTE—The term "perivalvular" is deprecated.

3.40 probability: Statistical likelihood that a specific event will occur.

3.41 process validation: Establishing, by objective evidence, that a process consistently produces a result or product that meets its predetermined specifications.

3.42 profile height: Maximal axial dimension of a heart valve substitute in the open or closed position, whichever is greater.

3.43 prosthetic valve endocarditis: Infection involving a heart valve substitute.

NOTE—Diagnosis is based on customary clinical criteria, including an appropriate combination of positive blood cultures, clinical signs (fever, new or altered cardiac murmurs, splenomegaly, systemic embolus, or immunopathologic lesions), and/or histologic confirmation of endocarditis at reoperation or autopsy. Morbidity associated with active infection such as valve thrombosis, embolus, or paravalvular leak is included under this category and is not included in other categories of morbidity.

3.44 quasi-real time durability testing: Long-term durability testing performed at a cycle rate between normal and high normal (up to 200 cycles/min).

3.45 reference valve: Heart valve substitute used to assess the conditions established in the *in vitro* tests used to evaluate the test heart valve substitute.

NOTE—The reference valve should approximate the test heart valve substitute in type, configuration, and tissue annulus diameter; it may be an earlier model of the same valve, if it fulfills the necessary conditions. The characteristics of the reference valve should be well documented with clinical data.

3.46 regurgitant fraction: Regurgitant volume expressed as a percentage of the stroke volume.

3.47 regurgitant volume: Volume of fluid that flows through a heart valve substitute in the reverse direction during one cycle and is the sum of the closing volume and the leakage volume. See Figure 1.

3.48 rigid heart valve substitute: Heart valve substitute wherein the occluder(s) and orifice ring are non-flexible under physiological conditions.

NOTE—This category was previously known as mechanical heart valve substitute. Materials of construction of the rigid components of rigid heart valve substitutes have historically been metals, pyrolytic carbon, and polymers.

3.49 risk: Combination of the probability of occurrence of harm and the severity of that harm (ISO/IEC Guide 51:1999[14], definition 3.2).

3.50 risk analysis: Systematic use of available information to identify hazards and to estimate the associated risks.

NOTE—Adapted from ISO/IEC Guide 51:1999[14], definition 3.10.

3.51 risk assessment: Overall process comprising a risk analysis and a risk evaluation (ISO/IEC Guide 51:1999[14], definition 3.12).

3.52 risk control: Process through which decisions are reached and protective measures are implemented for reducing risks to, or maintaining risks within, specified levels.

3.53 risk estimation: Process used to assign values to the probability and consequences of a risk.

3.54 risk evaluation: Judgment, on the basis of risk analysis, of whether an acceptable level of risk has been achieved in a given context based on the current values of society.

NOTE—Adapted from ISO/IEC Guide 51:1999[14], definitions 3.7 and 3.11.

3.55 risk management: Systematic application of management policies, procedures, and practices to the tasks of analyzing, evaluating, and controlling risk.

3.56 root mean square forward flow (RMS forward flow): Square root of the integral of the volume flow waveform squared.

NOTE 1—This is calculated using Equation (1).

$$q_{v\,RMS} = \sqrt{\frac{\int_{t_1}^{t_2} q_v(t)^2 dt}{t_2 - t_1}} \qquad (1)$$

where

$q_{v\,RMS}$ is root mean square forward flow;

$q(t)$ is instantaneous flow at time t;

t_1 is time at start of forward flow;

t_2 is time at end of forward flow.

NOTE 2—The rationale for use of $q_{v\,RMS}$ is that the instantaneous pressure difference is proportional to the square of instantaneous flow rate, and it is the mean pressure difference that is required.

3.57 safety: Freedom from unacceptable risk (ISO/IEC Guide 51:1999[14], definition 3.1).

3.58 severity: Measure of the possible consequences of a hazard.

3.59 simulated cardiac output: Net fluid volume forward flow per minute, through a test heart valve substitute.

3.60 special processes: Those processes for which the product cannot be fully verified by inspection or test.

3.61 sterile: Free from viable micro-organisms.

3.62 sterility assurance level (SAL): Probability of a viable micro-organism being present on a product after sterilization.

3.63 sterilization: Validated process used to render a product free from all forms of viable micro-organisms.

3.64 stroke volume: Volume of fluid moved through a test heart valve substitute in the forward direction during one cycle.

3.65 structural deterioration: Change in the function of a heart valve substitute resulting from an intrinsic abnormality that causes stenosis or regurgitation.

NOTE—This definition excludes infection or pannus overgrowth, or thrombosis of the heart valve substitute as determined by reoperation, autopsy, or *in vivo* investigation. It includes intrinsic changes such as wear, fatigue failure, stress fracture, occluder escape, calcification, cavitation erosion, leaflet tear, and stent creep.

3.66 supra-annular sewing ring: Sewing ring designed to secure the valve wholly above the patient's tissue annulus. See Figure 2.

3.67 systemic embolism: Clot or other particulate matter, not associated with infection, originating on or near the heart valve substitute and transported to another part of the body.

NOTE—Diagnosis may be indicated by a new, permanent or transient, focal or global neurologic deficit (exclusive of hemorrhage), or by any peripheral arterial embolus unless proved to have resulted from another cause (e.g., atrial myxoma). Patients who do not awaken post-operatively or who awaken with a stroke or myocardial infarction are excluded. Acute myocardial infarction that occurs after operation is arbitrarily defined as an embolic event in patients with known normal coronary arteries or who are less than 40 y of age.

3.68 tissue annulus diameter (TAD): Diameter in millimeters of the smallest flow area within the patient's valve annulus.

3.69 validation: Confirmation by examination and provision of objective evidence that the particular requirements for a specific intended use can be consistently fulfilled.

3.70 valve size: Manufacturer's designation of a heart valve substitute which indicates the tissue annulus diameter (TAD in millimeters) of the patient into whom the heart valve substitute is intended to be implanted (i.e., TAD = designated valve size).

NOTE—This takes into consideration the manufacturer's recommended implant position relative to the annulus and the suture technique. See also A.7, Q.2.2 c), Q.2.3 b), and Q.2.3 g).

3.71 valve thrombosis: Blood clot, not associated with infection, causing dysfunction of the heart valve substitute.

NOTE—Diagnosis may be proved by operation, autopsy, or clinical investigation (e.g., echocardiography, angiocardiography, or magnetic resonance imaging).

3.72 verification: Confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.

4 Abbreviations

For the purposes of this document, the following abbreviations apply.

A_{BS}	Body Surface Area
A_{EO}	Effective Orifice Area
AF	Atrial Fibrillation
ALARP	As Low As Reasonably Practicable
AWT	Accelerated Wear Testing
BSE	Bovine Spongiform Encephalopathy
CFD	Computational Fluid Dynamics
ECG	Electrocardiogram
ESRD	External Sewing Ring Diameter
FEA	Finite Element Analysis
FMEA	Failure Mode and Effect Analysis
FTA	Fault Tree Analysis
IFU	Instructions For Use
INR	International Normalized Ratio

IOA Internal Orifice Area
OPC Objective Performance Criteria
PROB Probability Rating
RIND Reversible Ischemic Neurological Deficits
RPN Risk Priority Number = SEV x PROB
SEV Hazard Severity Rank
SEM Scanning Electron Microscopy

5 Fundamental requirements

The manufacturer shall determine, at all stages of the product life cycle, the acceptability of the product for clinical use. The requirements of ISO 14971 and ISO 13485 shall apply.

6 Device description

6.1 Intended use

The manufacturer shall identify the physiological condition(s) to be treated, the intended patient population, potential adverse events, and intended claims.

6.2 Design inputs

6.2.1 Operational specifications

The manufacturer shall define the operational specifications for the device, including the principles of operation, expected device lifetime, shelf life, shipping/storage limits, and the physiological environment in which it is intended to function. Table 1 defines the expected physiological parameters of the intended patient population for heart valve substitutes for both normal and pathological patient conditions.

Table 1—Heart valve substitute operational environment

Parameter	Description			
Surrounding medium:	Human heart/Human blood			
Temperature:	34 °C to 42 °C			
Heart rate:	30 beats/min to 200 beats/min			
Cardiac output:	3 l/min to 15 l/min			
Stroke volume:	25 ml to 100 ml			
Blood pressures and resultant pressure loads by patient condition:	Arterial peak systolic pressure mm Hg	Arterial diastolic pressure mm Hg	Differential pressure across closed valve	
			Aortic Δp_A mm Hg	Mitral Δp_M mm Hg
Normotensive	100 to 130	65 to 85	95	115
Hypotensive	60	40	50	60
Hypertensive				
Stage 1 (mild)	140 to 159	90 to 99	123	150
Stage 2 (moderate)	160 to 179	100 to 109	138	170
Stage 3 (severe)	180 to 209	110 to 119	155	195
Stage 4 (very severe)	> 210	> 120	185	210
Extreme (expected maximum pressure for a single cycle)	300	160	230	300

Annex L
(informative)

Guidelines for verification of hydrodynamic performance

L.1 General

This annex provides guidance on test equipment, test equipment validation, formulation of test protocols, and test methods for the hydrodynamic performance of heart valves.

L.2 Steady forward-flow testing

L.2.1 Measuring equipment accuracy

L.2.1.1 Pressure measurement system should have a measurement accuracy of at least ± 0.26 kPa (± 2 mm Hg).

L.2.1.2 All other measurement equipment should have a measurement accuracy of at least ± 5 % of the full-scale reading.

L.2.2 Test apparatus requirements

L.2.2.1 Steady flow testing for aortic and mitral heart valve substitutes should be conducted in a straight tube having an internal diameter of 35 mm.

L.2.2.2 The test system should be capable of generating flow rates of at least 30 l/min.

L.2.2.3 Flow entering the test chamber should be relatively non-disturbed; this can be achieved by use of a flow staightener upstream of the heart valve substitute.

L.2.2.4 Pressure taps should be located one tube diameter upstream and three tube diameters downstream from the midplane of the heart valve substitute sewing ring. If sufficient data can be provided to demonstrate comparable results, other pressure tap configurations may be used.

L.2.2.5 Pressure taps should be flush with the inner wall of the tube.

L.2.2.6 A standard nozzle in accordance with Figure L.1 should be used to characterize the forward flow pressure and flow measuring equipment.

L.2.3 Test procedure

Measure the difference across the test valve and the standard nozzle over a flow rate range of 5 l/min to 30 l/min in 5 l/min increments.

L.2.4 Test report

The test report should include:

a) a description of the fluid used for the test, including its biological origin or chemical components, temperature, viscosity specific gravity;

b) a description of the steady flow apparatus;

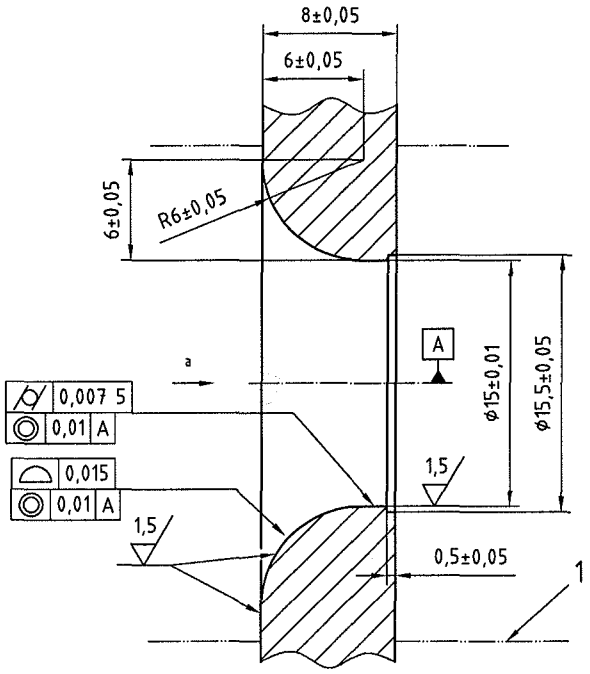
c) details of the mean values and standard deviation of the following performance test variables at each simulated condition for each test heart valve substitute and standard nozzle should be presented in tabular and graphic form:

   1) steady flow rate;

   2) pressure differences;

   3) effective orifice area.

Dimensions in millimeters.



Key
1 Wall of model vessel
a Flow direction

Figure L.1—Standard nozzle; forward flow

L.3 Steady back-flow leakage testing

L.3.1 Measuring equipment accuracy

L.3.1.1 Steady flow leakage flowrate should have a minimum measurement accuracy of ± 1 ml/s.

L.3.1.2 All other measuring equipment should have a minimum measurement accuracy of ± 5 % of the full-scale reading.

L.3.2 Test apparatus requirements

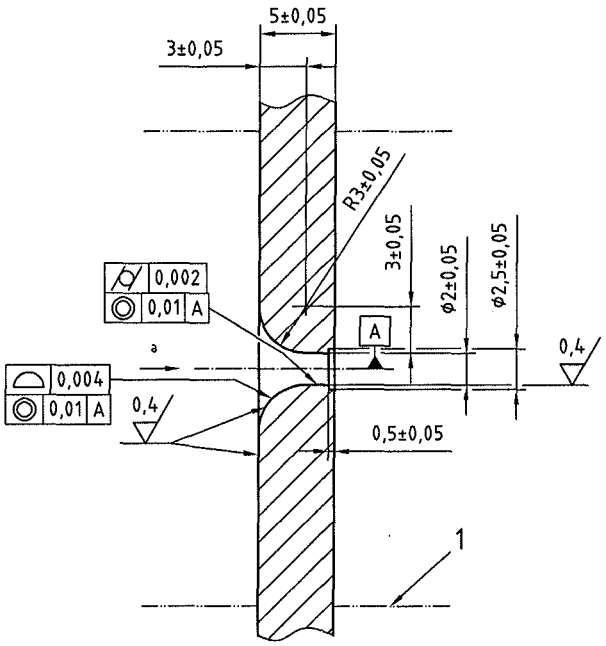
L.3.2.1 The steady backflow leakage testing should be conducted in an apparatus that is capable of generating constant backpressures in the range of 5.2 kPa to 26 kPa (40 mm Hg to 200 mm Hg).

L.3.2.2 The heart valve substitute should be mounted in such a manner as to minimize leakage around and through the sewing ring.

L.3.2.3 A standard nozzle in accordance with Figure L.2 should be used to characterize the backpressure, leakage volume flow rate, and pressure-measuring equipment.

L.3.2.4 The repeatability of the test system should be evaluated and documented.

Dimensions in millimeters.



Key
1 Wall of model vessel
a Flow direction

Figure L.2—Standard nozzle; backflow

L.3.3 Test procedure

Measure the static leakage across the test valve and the standard nozzle at five equidistant back pressures in the range of 5.2 kPa to 26 kPa (40 mm Hg to 200 mm Hg). Collect at least five measurements at each level of back pressure.

L.3.4 Test report

The steady backflow test report should include:

a) a description of the fluid used for the test, including its biological origin or chemical components, temperature, viscosity, and specific gravity under the test conditions;

b) a description of the steady flow apparatus;

c) details of the mean, range, and standard deviation of the performance test variables, at each simulated condition for each test heart valve substitute and standard nozzle, presented in tabular and graphic form; i.e., static leakage volume flow rate, expressed in l/min, as a function of back pressure.

L.4 Pulsatile-flow testing

L.4.1 Measuring equipment accuracy

L.4.1.1 The pressure measurement system should have a natural frequency of at least 20 Hz and a measurement accuracy of at least ± 0.26 kPa (± 2 mm Hg).

L.4.1.2 Regurgitant volume measurements should have a measurement accuracy of at least ± 2 ml.

L.4.1.3 All other measuring equipment should have a measurement accuracy of at least ± 5 % of the full-scale reading.

L.4.2 Test apparatus requirements

L.4.2.1 Pulsatile-flow testing should be conducted in a pulse duplicator that produces pressure and flow waveforms that approximate physiological conditions over the required physiological range.

L.4.2.2 The pulse duplicator should have had its properties and performance established by means of testing reference valves of different sizes in both the aortic and mitral positions.

L.4.2.3 The pulse duplicator should permit measurement of time-dependent pressures, volumetric flow rates, velocity fields, and turbulent shear stress fields.

L.4.2.4 The repeatability of the test system should be evaluated and documented.

L.4.2.5 Relevant dimensions of the cardiac chambers and vessels should be simulated.

L.4.2.6 In cases where the compliance may affect the pressure difference or regurgitation characteristics of the valve (e.g., the aortic compliance in an unstented aortic valve), the relevant chamber compliance should be simulated (see Annex F for guidelines on compliant chambers).

L.4.2.7 The chamber should allow the observer to view and photograph the test heart valve substitute at all stages of the cycle.

L.4.3 Test procedure

L.4.3.1 Tests should be carried out on each valve in the position in which it is intended to be used. Qualitative and quantitative assessments should be made.

L.4.3.2 Pressure difference should be measured at four simulated cardiac outputs between 2 l/min and 7 l/min (e.g., 2 l/min, 3.5 l/min, 5 l/min, 7 l/min), at a single simulated normal heart rate (e.g., 70 cycles/min).

L.4.3.3 Regurgitant volumes should be measured at three different mean (averaged over the cardiac cycle) back pressures (e.g., 10.4 kPa, 15.6 kPa, and 20.8 kPa (80 mm Hg, 120 mm Hg, and 160 mm Hg)), at three simulated low, normal, and high heart rates (e.g., 45 cycles/min, 70 cycles/min, and 120 cycles/min) at a normal simulated cardiac output (e.g., 5 l/min).

L.4.3.4 At least ten measurements of each of the following variables should be obtained from either consecutive or randomly-selected cycles:

a) mean pressure difference across the test heart valve substitute;

b) mean and RMS flow rates through the test heart valve substitute;

c) stroke volume;

d) cycle rate;

e) mean arterial pressure over the whole cycle;

f) duration of forward flow through the test heart valve substitute, as a percentage of cycle time;

g) regurgitant volume, including the closing volume, the leakage volume (see Figure 1), and the corresponding mean pressure difference across the closed valve.

L.4.3.5 Assess the flow fields (velocity and shear) in the immediate vicinity of the heart valve substitute, including within the valve "housing" mechanism (e.g., within the hinge region of a bileaflet rigid valve design). Techniques for such measurements include laser Doppler velocimetry (LDV), digital particle image velocimetry (DPIV), and computational fluid dynamics (CFD). CFD code should be validated by comparison with experimental results. State-of-the-art CFD techniques should be used to validate the code and its application to the valve design being evaluated.

L.4.3.6 Quantitatively assess the hemolytic and thrombogenic potential of the valve design in each position of intended use, either in the studies described in L.4.3.5, or other relevant *in vitro*, computational, and/or *in vivo* studies. Measures such as shear rate magnitude versus duration and particle residence time should be considered.

L.4.4 Test report

The pulsatile-flow test report should include the following information:

a) a description of the fluid used for the test, including its biological origin or chemical components, temperature, viscosity, and specific gravity under the test conditions;

b) a description of the pulse duplicator, as specified in L.4.2, and its major components and associated apparatus, including a schematic diagram of the system giving the relevant chamber dimensions, chamber compliance (if a compliant chamber is used), details of the location of the pressure-measuring sites relative to the mid-plane of the heart valve substitute sewing ring, pressure measurement instrumentation frequency response, and the appropriate representative pressure and flow waveforms at approximately 70 cycles/min, simulated cardiac output of 5 l/min and mean arterial pressure of 13 kPa (100 mm Hg);

c) an assessment, including appropriate documentation, of the opening and closing action of a test heart valve substitute and, if appropriate, its adjacent flow field under stated conditions;

d) a permanent recording of at least ten consecutive or randomly selected cycles of the time-dependent simultaneous pressures, proximal and distal to the heart valve substitute, and the volume flow through it. Details of mean, range, and standard deviation of the performance test variables (e) to (p) at each simulated cardiac output for each test heart valve substitute and reference valve should be presented in tabular and graphic form;

e) simulated cardiac output;

f) cycle rate;

g) duration of forward-flow phase, expressed as a percentage of the cycle time;

h) stroke volume;

i) mean and RMS flow rates;

j) mean pressure difference;

k) effective orifice area (provide formula used);

l) regurgitant volume, closing volume, and leakage volume, expressed in milliliters and as a percentage of stroke volume; the corresponding mean pressure difference across the closed valve;

m) mean arterial pressure over the whole cycle;

n) appropriate qualitative photographic documentation and quantitative analyses of the opening and closing characteristics for the heart valve substitute;

o) appropriate documentation and quantitative analyses of the velocity and shear stress fields in the immediate vicinity, including where appropriate within the valve "housing";

p) appropriate qualitative and quantitative documentation for the hemolytic and thrombogenic potential.